12

TOPICAL HAZARD EVALUATION
OF
CANDIDATE INSECT REPELLENT AI3-35713-aGa
N-PENTYLVALERAMIDE

STUDY NO. 51-0802-77

AUGUST 1975 - AUGUST 1976

Approved for public release; distribution unlimited

US ARMY
ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MD 21010

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Date Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: 51-0802-77 (76)
2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER

4. TITLE (and Subtitle): Topical Hazard Evaluation of Candidate Insect Repellent AI3-35713-aGa N-Pentylvaleramide
5. TYPE OF REPORT & PERIOD COVERED: Aug 75 - Aug 76
6. PERFORMING ORG. REPORT NUMBER

7. AUTHOR(s): (10) K. Clark/Swentzel
8. CONTRACT OR GRANT NUMBER(s)

9. PERFORMING ORGANIZATION NAME AND ADDRESS: US Army Environmental Hygiene Agency, Aberdeen Proving Ground MD 21010
10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: (11) 17 Oct 76

11. CONTROLLING OFFICE NAME AND ADDRESS: Commander, US Army Health Services Command, Fort Sam Houston, TX 78234
12. REPORT DATE: (12) 8 p.
13. NUMBER OF PAGES: 6

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): (14) USAEHA-51-0802-77
15. SECURITY CLASS. (of this report): UNCLASSIFIED
15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

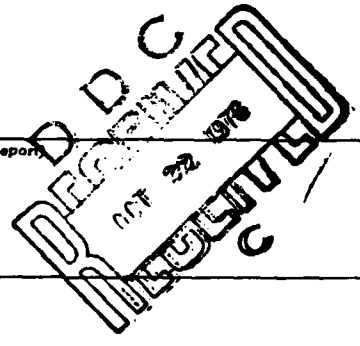
16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited

(9) Topical hazard evaluation rept.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

Aug 75 - Aug 76



18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

approximate lethal dose
Topical Hazard Evaluation
insect repellent
skin irritation
New Zealand White rabbits
Sprague-Dawley
N-Pentylvaleramide
skin sensitization
eye irritation
photochemical
Wistar-derived rats
guinea pigs
AI3-35713-aGa

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

An evaluation of AI3-35713-aGa was conducted using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. It is recommended that AI3-35713-aGa be approved for further testing as a candidate insect repellent.

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

038150

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Date Entered)

(B)

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT/WP

19 OCT 1976

TOPICAL HAZARD EVALUATION
OF
CANDIDATE INSECT REPELLENT AI3-35713-aGa
N-PENTYLVALERAMIDE
STUDY NO. 51-0802-77
AUGUST 1975 - AUGUST 1976

1. AUTHORITY.

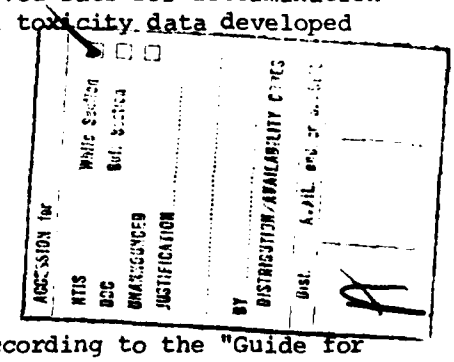
a. Letter, US Department of Agriculture, Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, FL, 14 August 1975.

b. Memorandum of Understanding Between the US Department of the Army, Office of The Surgeon General, the US Army Health Services Command, the US Army Environmental Hygiene Agency, the Army Forces Pest Control Board and the US Department of Agriculture, effective December 1970 with Amendment No. 1, effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972.

3. PURPOSE. The purpose of this study was to provide guidance for further entomological testing of the candidate insect repellent AI3-35713-aGa.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-35713-aGa (N-Pentylvaleramide) was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*



* The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," as prepared by the Committee on Revision of the "Guide for Laboratory Animal Facilities and Care," of the Institute of Laboratory Animal Resources, National Research Council (1972).

Study No. 51-0802-77, Aug 75 - Aug 76

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.		
0.5 ml technical grade compound applied to each of six rabbits.	AI3-35713-aGa produced very slight erythema at 24 hours and very slight to slight edema at 24 and 72 hours at the abraded skin sites in three of six rabbits.	USAEHA Category I (ref Appendix). There is no restriction for acute application to the human skin.
0.5 ml solvent (acetone) applied to each of six rabbits.	Acetone produced very slight erythema at 24 hours in one of six rabbits at the abraded skin site.	
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	AI3-35713-aGa produced no irritation to the eyes.	USAEHA Category A (ref Appendix). Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

Study No. 51-0802-77, Aug 75 - Aug 76

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single application (0.05 ml) of a 25 percent (w/v) solution of the compound and of a 10 percent (w/v) oil of Bergamot solution (positive control) in 95 percent ethyl alcohol, were applied to the intact skin of six New Zealand White rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes from a distance of 10 to 15 cm. Application area was checked for irritation at 24, 48, and 72 hours.	AI3-35713-aGa did not cause a photochemical irritation reaction under test conditions.	AI3-35713-aGa did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical reaction in humans.
Control		
Following UV exposure of the rabbits, 0.05 ml of the test compound, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites.	Positive control application and irradiation caused greater irritant effects than in unirradiated areas.	
APPROXIMATE LETHAL DOSE		
Oral		
Rats (male) - corn oil diluent	ALD 4311 mg/kg	Presents little lethal hazard from acute accidental ingestion.

Study No. 51-0802-77, Aug 75 - Aug 76

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SENSITIZATION STUDIES		
Guinea Pigs (male)		
Intradermal injections of 0.1 ml of a 0.1 percent solution (w/v) of AI3-35713-aGa or of a 0.1 percent suspension of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs receiving and challenged with a 0.1 percent solution of AI3-35713-aGa.	Challenge dose of AI3-35713-aGa (last intradermal injection) produced no greater irritation reaction than that observed on the cage control animals.	AI3-35713-aGa did not sensitize guinea pigs and is not expected to cause a sensitization reaction in humans.
Ten positive control guinea pigs receiving and challenged with a 0.1 percent suspension of DNCB.	Positive control (DNCB) produced sensitization in ten of ten guinea pigs.	
Ten cage control guinea pigs Five receiving challenge dose of AI3-35713-aGa at 0.1 percent without prior sensitizing doses. Five receiving challenge dose of DNCB at 0.1 percent without prior sensitizing doses.		

* A known skin sensitizer.

5. CONCLUSION. AI3-35713-aGa did not produce a positive irritation reaction in any of these tests and is not expected to be an acute topical toxic hazard when handled by humans.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (reference paragraph 1b), it is recommended that AI3-35713-aGa be approved for further testing as a candidate insect repellent.

K. CLARK SWENTZEL
Biologist
Toxicology Division

DONALD L. BUMGARDNER
SSG
Veterinary Specialist
Toxicology Division

APPROVED:

ARTHUR H. McCREESH, Ph.D.
Chief, Toxicology Division

JOHN F. MAZUR
MAJ, MSC
Acting Director, Laboratory Services

APPENDIX

TOPICAL HAZARD EVALUATION
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals. prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.